

**REMARKS/ARGUMENTS**

Applicants respectfully request reconsideration and allowance of this application in view of the amendments above and the following comments.

Claims 17-46, 48 and 53-55 were rejected under 35 USC § 101 as being directed to non-statutory subject matter. In response, Applicants have limited the claims without prejudice to non-human mammalian cells and mammals.

Claims 17-46, 48 and 53-55 were rejected under 35 USC § 112, first paragraph, as being broader than the enabling disclosure. The Examiner concedes enablement for "mammals." Accordingly, in order to advance the prosecution, Applicants have limited the claims without prejudice to non-human mammalian cells and mammals.

Claims 17-46, 48 and 53-55 were rejected under 35 USC § 112, second paragraph, as being indefinite. In response, Applicants submit that the claims as amended above are definite.

According to the Examiner, claim 18 is indefinite because it is unclear how the targeting vector relates to the "functional DNA sequence" or "gene expression cassette" in claim 17. Applicants respectfully disagree. Claim 18 recites "*said* functional DNA sequence." Therefore, it is clear that the functional DNA sequence in claim 18 is the same functional DNA sequence recited in claim 17 since the only antecedent basis for "said functional DNA sequence" in claim 18 is the functional DNA sequence in claim 17. Further, the functional DNA sequence in claim 17 is stated to be either the gene expression cassette or a DNA sequence that can be converted to the gene expression cassette. So, it is also clear that the functional DNA sequence in claim 18 is

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also either the gene expression cassette or the DNA sequence that can be converted to the gene expression cassette. Claim 18 merely adds the additional requirement that the functional DNA sequence of claim 17 is flanked by DNA sequences homologous to the Rosa26 locus and this combination forms the targeting vector.

According to the Examiner, claims 18 and 19 are unclear in attempting to limit how the functional DNA sequence is introduced while simultaneously attempting to further limit the structure of the functional DNA sequence. In response, Applicants have amended claims 18 and 19 to separate the clauses.

According to the Examiner, claim 19 was unclear because "site specific recombinase mediated recombination" was unknown. In response, Applicants point out that the technique was, in fact, well known in the art. The specification references the technique at the bottom of page 9 and the top of page 10. A reference is also given there to a 1992 article by Fukushima et al., *Pro. Nat. Aca. Sci. USA*, 89: 7905-9. And, US 7,205,148 at column 2, lines 3-4, specifically mentions "site specific recombinase mediated recombination." Clearly, this technique is well known in the art and, therefore, persons skilled in the art understand what is being claimed in claim 19.

According to the Examiner, claim 28 is indefinite because "primary cells" are not defined in the specification and are unknown in the art. Again, Applicants respectfully disagree. A brief search of the USPTO website reveals some 415 patents referring to "primary cells" and "immortalized cells." Respectfully, persons skilled in the art are quite familiar with these terms and claim 28 is not indefinite.

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According to the Examiner, claim 30 is indefinite because “pharmaceutically active” is unclear. Again, Applicants respectfully disagree. A brief search of the USPTO website reveals some 1427 patents with claims reciting “pharmaceutically active.” Respectfully, persons skilled in the art fully understand the phrase “pharmaceutically active,” and, therefore, know what is and is not encompassed by claim 30.

According to the Examiner, claim 31 is indefinite in the recitation of “heterologous promoter.” In response, Applicants have specified that the heterology is relative to the Rosa26 locus.

According to the Examiner, claims 32 and 33 are indefinite in the use of generic and specific promoters. In response, Applicants respectfully submit that these are all well known promoter genera and species. In any case, the specification provides sources in the first paragraph on page 8.

With respect to claims 34 and 35, Applicants have amended these claims to provide all necessary antecedent basis and to delete the extraneous references to “functional.”

According to the Examiner, the phrase “DNA sequences homologous to the Rosa26 locus” in claim 36 lacks antecedent basis. However, the phrase clearly appears in the last two lines of claim 18, from which claim 36 depends.

With respect to claim 38, Applicants have removed the reference to “transgenic,” thereby mooting the lack of antecedent basis issue. Applicants have also deleted the references to “derived.”

With respect to claim 39, Applicants have deleted "respectively."

With respect to claim 40, Applicants have deleted "derived."

With respect to claim 42, Applicants have replaced this claim by new claim 56, which is believed to overcome each of the Examiner's concerns.

According to the Examiner, claim 45 is indefinite in the recitation of "an inactive positive selection marker." Again, Applicants respectfully submit these markers are well known to persons skilled in the art. Moreover, the specification gives examples at page 10, second paragraph, under "(iii)."

With respect to claim 46, Applicants have labeled the two steps as (a) and (b). It is clear that these two steps are after the step indicated in claim 17 since these two steps begin with the transgenic cells that are the result of the step indicated in claim 17. Also, Applicants have removed the references to "preferred," "desired" and "integrated."

With respect to claim 48, the Examiner says it cannot be determined how claim 17 further limits the claims. In response, Applicants have provided that the eukaryotic cells are obtained by the process of claim 17.

Finally, Applicants have amended claims 53-55 to provide allegedly "missing" steps.

In view of the foregoing, Applicants respectfully submit that the claims are definite. An early notice to that effect is earnestly solicited.

Claims 17-25, 28-32, 34-38, 42-46, 48 and 53-55 were rejected under 35 USC § 102(b) as

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being anticipated by Soriano, WO 99/53017. In response, Applicants remind the Examiner that anticipation requires that each and every element as set forth in the claim must be found, either expressly or inherently described, in a single prior art reference, and, further, the absence in the prior art reference of even a single one of the claim elements is sufficient to negate anticipation. *In re Robertson*, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999). The Examiner concedes that Soriano teaches a LacZ gene under the control of the mouse Rosa26 promoter. In contrast, the instant claims require that the gene expression cassette comprises "a gene of interest operatively linked to a promoter." This gene expression cassette is then required to be introduced into the eukaryotic cell, which means that the promoter is, therefore, exogenous to the eukaryotic cell. Further, although claim 17 allows for the introduction of "a DNA sequence which can be converted into such gene expression cassette," since the gene expression cassette comprises an exogenous promoter, the convertible DNA sequence must likewise contain an exogenous promoter, otherwise it cannot be converted into the gene expression cassette containing such exogenous promoter. Consequently, Soriano does not, in fact, teach the present invention.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this rejection as well. An early notice that this rejection has been reconsidered and withdrawn is earnestly solicited.

Applicants believe that the foregoing constitutes a bona fide response to all outstanding objections and rejections.

Applicants also believe that this application is in condition for immediate allowance. However, should any issue(s) of a minor nature remain, the Examiner is respectfully requested to

telephone the undersigned at telephone number (212) 808-0700 so that the issue(s) might be promptly resolved.

Early and favorable action is earnestly solicited.

Respectfully submitted,  
NORRIS McLAUGHLIN & MARCUS, P.A.

By /Kurt G. Briscoe/  
Kurt G. Briscoe  
Attorney for Applicant(s)  
Reg. No. 33,141  
875 Third Avenue  
18<sup>TH</sup> Floor  
New York, New York 10022  
Phone: (212) 808-0700  
Fax: (212) 808-0844

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